REMARKS/ARGUMENTS

Claims 1-63 are pending in this application. Claims 1-53, 55-56 and 58-63 have been canceled. Claims 54 and 57 have been amended.

The present application is a divisional of parent application No. 09/580,882, filed May 30, 2000. The '882 application was filed with claims 1-63. Claims 1-53 and 59-63 were allowed in the parent application and have since issued as claims 1-58 of U.S Patent No. 6,291,454, issued September 18, 2001. Accordingly, claims 1-53-59-63 have been canceled from the present application. As set forth above, claims 55-56 and 58 have also been canceled. Thus, the only claims remaining in this divisional application are claims 54 and 57.

The cancellation of claims 1-53, 55-56 and 58-63 has rendered the various grounds of rejection of these claims moot.

As to remaining claims 54 and 57, these claims have been rejected under 35 U.S.C. § 112, second paragraph, as incomplete entities. To address this rejection, claim 54 has been amended to incorporate the compounds defined by original claims 1 and 43 from the parent application. These claims were allowed in the parent application and have issued as claims 1 and 43 of U.S. Patent No. 6,291,454. Claims 57 has been amended to depend from claim 54 and, as such, includes all of the limitations of independent claim 54. In view of these amendments, applicants believe that the rejection of claims 54 and 57 under the second paragraph of § 112 as incomplete entities has been traversed.

Claims 54 and 57 have also been rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. While applicants do not agree with the Examiner's position that these claims are not enabled, applicants have, in an effort to advance prosecution, amended claim 54 to recite hypersensitivity, allergy, asthma and bronchospasm as the disorders being treated. The method of claim 57 relates specifically to the treatment of asthma.

The disclosure fully enables those skilled in the art to practice the claimed methods. The use of dihydropyridine-type calcium channel blockers in treating disorders such as hypersensitivity, allergy, asthma and bronchospasm is well-known in the art, as established by the art already of record in this application. It is further noted that because the compounds administered according to the claimed method of treatment are short acting they exert their effects locally. Thus, these compounds, when administered locally to the lungs, are particularly effective for treating the enumerated disorders. The specification at, for example, page 13, lines

12-24, discloses a number of formulations for administering these compounds to the lungs via inhalation, including a solution intended for administration by metered dose inhaler , or in a form suitable for a dry powder inhaler or insufflator. Typically, administration via inhalation is accomplished by delivering the specified compounds in the form of an aerosol spray from a pressurized container using a suitable propellant and a valve to deliver a metered dose, as is pointed out in the specification and as is well-known in the art.

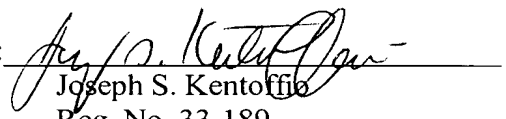
In view of the scope of the disclosure and the level of skill in the art with respect to the use of dihydropyridine-type calcium channel blockers, applicants submit that method of treatment claims 54 and 57 are fully enabled. Accordingly, applicants request that the rejection of claims 54 and 57 under 35 U.S.C. § 112, first paragraph, be withdrawn and that a Notice of Allowance with respect to these claims be issued at the earliest possible date.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned "Version With Markings To Show Changes Made".

Applicants do not believe that any fees are required in connection with the filing of this Response. However, should any such fees be required please charge Deposit Account No. 10-0750/ORT-1477/JSK.

Should the Examiner have any questions regarding this Response, please contact the undersigned attorney at the telephone number listed.

Respectfully submitted,

By: 
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Dated: June 26, 2002

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Please insert the following new paragraph after the title but before Field of the Invention:

-- **Related Applications**

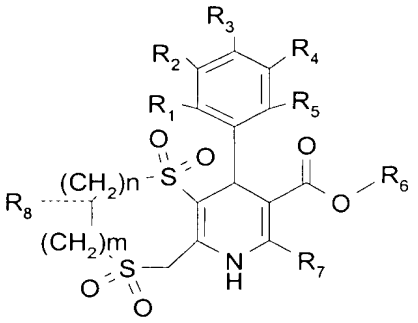
This divisional application claims the benefit under 35 U.S.C. § 119(e) of provisional application Serial No. 60/138,987, filed June 14, 1999. This application also claims the benefit under U.S.C. § 120 of parent application Serial No. 09/580,882, filed on May 30, 2000, now issued as US Patent No. 6,291,454. --

In the Claims:

Please amend claims 54 and 57 as follows:

54. (amended) A method of treating a subject suffering from a disorder [whose alleviation is mediated by the reduction of calcium ion influx into cells whose actions contribute to the disorder] selected from the group consisting of hypersensitivity, allergy, asthma and bronchospasm, which method comprises administering to the subject a therapeutically effective dose of [the] a pharmaceutical composition [of Claim 53] comprising a pharmaceutically acceptable carrier and a compound of Formula I or Formula II,

wherein Formula I is as follows:



Formula I

or a pharmaceutically acceptable salt thereof, wherein

(a) R_1, R_2, R_3, R_4 and R_5 are independently selected from the group consisting of H, OH, halogen, cyano, NO_2, alkyl, C_{1-8} alkoxy, C_{1-8} alkylsulfonyl, C_{1-4} carboalkoxy, C_{1-8} alkylthio, difluoromethoxy, difluoromethylthio, trifluoromethyl, and oxadiazole (formed by R_1 and R_2);

(b) R_6 is selected from the group consisting of H, C_{1-5} straight or branched alkyl, aryl, 3-piperidyl, N-substituted 3-piperidyl, N-substituted 2-pyrrolidinyl methylene, and substituted alkyl, wherein

said N-substituted 3-piperidyl and said N-substituted 2-pyrrolidinyl methylene may be substituted with C_{1-8} straight or branched chain alkyl or benzyl, and said substituted alkyl may be substituted with C_{1-8} alkoxy, C_{2-8} alkanoyloxy, phenylacetyloxy, benzoyloxy, hydroxy, halogen, p-tosyloxy, mesyloxy, amino, carboalkoxy or NR'R", wherein

(i) R' and R" are independently selected from the group consisting of H, C_{1-8} straight or branched alkyl, C_{3-7} cycloalkyl, phenyl, benzyl, and phenethyl, or
(ii) R' and R" together form a heterocyclic ring selected from the group consisting of piperidino, pyrrolidino, morpholino, thiomorpholino, piperazino, 2-thieno, 3-thieno, and an N-substituted derivative of said heterocyclic rings,

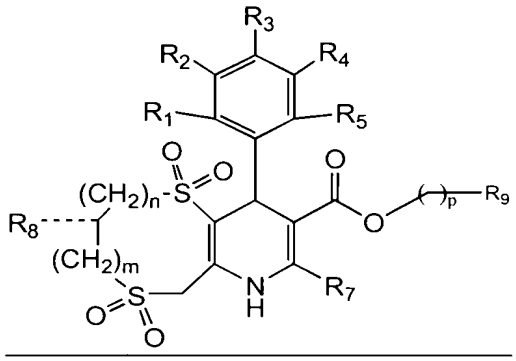
said N-substituted derivative being substituted with H, C_{1-8} straight or branched alkyl, benzyl, benzhydryl, phenyl and/or substituted phenyl (substituted with NO_2, halogen, C_{1-8} straight or branched chain alkyl, C_{1-8} alkoxy and/or trifluoromethyl);

(c) R_7 is selected from the group consisting of H, amino, alkyl, aryl, trifluoromethyl, alkoxymethyl, 2-thieno and 3-thieno;

(d) R_8 is connected to the bis-sulfone ring via a single or double bond, as applicable, and is selected from the group consisting of H, alkylhydroxy, alkenyl, amino, phenyl, benzyl, C_{1-8} straight or branched alkyl, trifluoromethyl, alkoxymethyl, C_{3-7} cycloalkyl, substituted benzyl, formyl, acetyl, t-butyloxy carbonyl, propionyl, substituted alkyl and R'''CH_2C=O, wherein (i) said substituted benzyl is substituted with halogen, trifluoromethyl, C_{1-8} straight and/or branched alkyl or C_{1-8} alkoxy, (ii) said substituted alkyl is substituted with amino, dialkyl amino, C_{1-8} alkoxy, hydroxy and/or halogen, and (iii) R''' is amino, dialkyl amino, C_{1-8} alkoxy, hydroxy or halogen; and

(f) m, n, and their sum are each an integer from 0 to 4;

and wherein Formula II is as follows:



Formula II

or a pharmaceutically acceptable salt thereof, wherein

(a) R_1, R_2, R_3, R_4 and R_5 are independently selected from the group consisting of H, OH, halogen, cyano, NO_2, alkyl, C_{1-8} alkoxy, C_{1-8} alkylsulfonyl, C_{1-4} carboalkoxy, C_{1-8} alkylthio, difluoromethoxy, difluoromethylthio, trifluoromethyl, and oxadiazole (formed by R_1 and R_2);

(b) R_7 is selected from the group consisting of H, amino, alkyl, aryl, trifluoromethyl, alkoxymethyl, 2-thieno and 3-thieno;

(c) R_8 is connected to the bis-sulfone ring via a single or double bond, as applicable, and is selected from the group consisting of H, alkylhydroxy, alkenyl, amino, phenyl, benzyl, C_{1-8} straight or branched alkyl, trifluoromethyl, alkoxymethyl, C_{3-7} cycloalkyl, substituted benzyl, formyl, acetyl, t-butyloxy carbonyl, propionyl, substituted alkyl and R'''CH_2C=O, wherein (i) said substituted benzyl is substituted with halogen, trifluoromethyl, C_{1-8} straight and/or branched alkyl or C_{1-8} alkoxy, (ii) said substituted alkyl is substituted with amino, dialkyl amino, C_{1-8} alkoxy, hydroxy and/or halogen, and (iii) R''' is amino, dialkyl amino, C_{1-8} alkoxy, hydroxy or halogen;

(d) R_9 is selected from -alkyl-OH, alkylamine, lactone, cyclic carbonate, alkyl-substituted cyclic carbonate, aryl-substituted cyclic carbonate, –aryl–C(O)OR', –alkyl-aryl–C(O)OR', –alkyl–OC(O)R', –alkyl–C(O)R', –alkyl–C(O)OR', –alkyl–N(R")C(O)R', and –alkyl–N(R")C(O)OR', wherein

R^I and R^{II} are independently selected from the group consisting of hydrogen, amino, alkyl, aryl, aryl-fused cycloalkyl, and heterocyclyl, the amino, alkyl, aryl, aryl-fused cycloalkyl, and heterocyclyl being optionally substituted with halogen, cyano, NO_2, lactone, amino, alkylamino, aryl-substituted alkylamino, amide, carbamate, carbamoyl, cyclic carbonate, alkyl, halogen-substituted

alkyl, arylalkyl, alkoxy, heterocyclyl and/or aryl (the aryl being optionally substituted with OH, halogen, cyano, NO_2, alkyl, amino, dimethylamino, alkoxy, alkylsulfonyl, C_{1-4} carboalkoxy, alkylthio and/or trifluoromethyl);

(e) m, n, and their sum are each an integer from 0 to 4; and

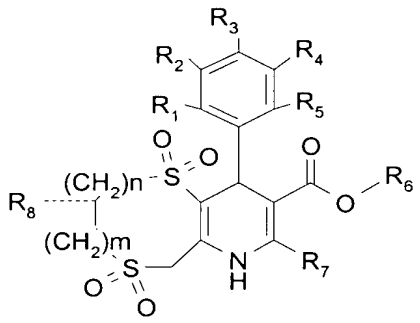
(f) p is an integer from 0 to 4.

57. (amended) The method of Claim [56] 54, wherein the disorder is asthma.

Please cancel claims 1-53, 55-56 and 58-63.

I

1. A compound of Formula I,



Formula I

or a pharmaceutically acceptable salt thereof, wherein

(a) R_1, R_2, R_3, R_4 and R_5 are independently selected from the group consisting of H, OH, halogen, cyano, NO_2, alkyl, C_{1-8} alkoxy, C_{1-8} alkylsulfonyl, C_{1-4} carboalkoxy, C_{1-8} alkylthio, difluoromethoxy, difluoromethylthio, trifluoromethyl, and oxadiazole (formed by R_1 and R_2);

(b) R_6 is selected from the group consisting of H, C_{1-5} straight or branched alkyl, aryl, 3-piperidyl, N-substituted 3-piperidyl, N-substituted 2-pyrrolidinyl methylene, and substituted alkyl, wherein

said N-substituted 3-piperidyl and said N-substituted 2-pyrrolidinyl methylene may be substituted with C_{1-8} straight or branched chain alkyl or benzyl, and said substituted alkyl may be substituted with C_{1-8} alkoxy, C_{2-8} alkanoyloxy, phenylacetyloxy, benzoyloxy, hydroxy, halogen, p-tosyloxy, mesyloxy, amino, carboalkoxy or NR'R", wherein

(i) R' and R" are independently selected from the group consisting of H, C_{1-8} straight or branched alkyl, C_{3-7} cycloalkyl, phenyl, benzyl, and phenethyl, or (ii) R' and R" together form a heterocyclic ring selected from the group consisting of piperidino, pyrrolidino, morpholino, thiomorpholino, piperazino, 2-thieno, 3-thieno, and an N-substituted derivative of said heterocyclic rings, said N-substituted derivative being substituted with H, C_{1-8} straight or branched alkyl, benzyl, benzhydryl, phenyl and/or substituted phenyl (substituted with NO_2, halogen, C_{1-8} straight or branched chain alkyl, C_{1-8} alkoxy and/or trifluoromethyl);

(c) R_7 is selected from the group consisting of H, amino, alkyl, aryl, trifluoromethyl, alkoxymethyl, 2-thieno and 3-thieno;

(d) R_8 is connected to the bis-sulfone ring via a single or double bond, as applicable, and is selected from the group consisting of H, alkylhydroxy, alkenyl, amino, phenyl, benzyl, C_{1-8} straight or branched alkyl, trifluoromethyl, alkoxymethyl, C_{3-7} cycloalkyl, substituted benzyl, formyl, acetyl, t-butyloxy carbonyl, propionyl, substituted alkyl and R'"CH_2C=O, wherein (i) said substituted benzyl is substituted with halogen, trifluoromethyl, C_{1-8} straight and/or branched alkyl or C_{1-8} alkoxy, (ii) said substituted alkyl is

substituted with amino, dialkyl amino, C_{1-8} alkoxy, hydroxy and/or halogen, and (iii) R''' is amino, dialkyl amino, C_{1-8} alkoxy, hydroxy or halogen; and

(e) m, n, and their sum are each an integer from 0 to 4.

2. The compound of Claim 1, wherein R_6 is $-(CH_2)_2N(CH_3)CH_2PH$.

3. The compound of Claim 1, wherein R_6 is methyl.

4. The compound of Claim 3, wherein R_4 is CF_3, R_5 is F, R_7 is methyl, R_8 is methylene, m is 0 and n is 1.

5. The compound of Claim 3, wherein R_4 is CF_3, R_5 is F, R_7 is methyl, R_8 is alkylhydroxy, m is 0 and n is 1.

6. The compound of Claim 1, wherein R_7 is methyl.

7. The compound of Claim 6, wherein R_6 is $-(CH_2)_2N(CH_3)CH_2PH$.

8. The compound of Claim 6, wherein R_4 is CF_3 and R_5 is F.

9. The compound of Claim 6, wherein R_5 is Cl.

10. The compound of Claim 6 wherein R_1 is F and R_5 is Cl.

11. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2-chloro-6-fluorophenyl)-2,3,6,9-tetrahydro-7-methyl-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,4,4-tetraoxide.

12. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 2,3,6,9-tetrahydro-7-methyl-9-(3,4,5-trifluorophenyl)-2-[methyl(2-thienylmethyl)amino]ethyl ester 1,1,4,4-tetraoxide.

13. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-[2-fluoro-6-(trifluoromethyl)phenyl]-2,3,6,9-tetrahydro-7-methyl-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,4,4-tetraoxide.

14. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2-chloro-6-fluorophenyl)-2,3,6,9-tetrahydro-7-methyl-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,4,4-tetraoxide, (9R).

15. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2-chloro-6-fluorophenyl)-2,3,6,9-tetrahydro-7-methyl-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,4,4-tetraoxide, (9S).

16. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2-chloro-6-hydroxyphenyl)-2,3,6,9-tetrahydro-7-methyl-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,4,4-tetraoxide.

17. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2-chlorophenyl)-2,3,6,9-tetrahydro-7-methyl-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,4,4-tetraoxide.

18. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-[2-fluoro-3-(trifluoromethyl)phenyl]-2,3,6,9-tetrahydro-7-methyl-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,4,4-tetraoxide.

19. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 2,3,6,9-tetrahydro-7-methyl-9-(3-nitrophenyl)-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,4,4-tetraoxide.

20. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 2,3,6,9-tetrahydro-7-methyl-9-(3,4,5-trifluorophenyl)-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,4,4-tetraoxide.

21. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2-chloro-6-fluorophenyl)-2,3,6,9-tetrahydro-7-methyl-methyl ester 1,1,4,4-tetraoxide.

22. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2-chloro-5-nitrophenyl)-2,3,6,9-tetrahydro-7-methyl-methyl ester 1,1,4,4-tetraoxide.

23. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 2,3,6,9-tetrahydro-7-methyl-9-(pentafluorophenyl)-methyl ester 1,1,4,4-tetraoxide.

24. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2,6-difluorophenyl)-2,3,6,9-tetrahydro-7-methyl-methyl ester 1,1,4,4-tetraoxide.

25. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2-chlorophenyl)-2,3,6,9-tetrahydro-7-methyl-methyl ester 1,1,4,4-tetraoxide.

26. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2-fluorophenyl)-2,3,6,9-tetrahydro-7-methyl-methyl ester 1,1,4,4-tetraoxide.

27. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-[2-fluoro-3-(trifluoromethyl)phenyl]-2,3,6,9-tetrahydro-7-methyl-methyl ester 1,1,4,4-tetraoxide.

28. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2,3-difluorophenyl)-2,3,6,9-tetrahydro-7-methyl-methyl ester 1,1,4,4-tetraoxide.

29. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 2,3,6,9-tetrahydro-7-methyl-9-(2-nitrophenyl)-methyl ester 1,1,4,4-tetraoxide.

30. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-[2-fluoro-3-(trifluoromethyl)phenyl]-2,3,6,9-tetrahydro-7-methyl-3-methylene-methyl ester 1,1,4,4-tetraoxide.

31. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-[2-fluoro-3-(trifluoromethyl)phenyl]-2,3,6,9-tetrahydro-7-methyl-3-methylene-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,4,4-tetraoxide.

32. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-[2-fluoro-3-(trifluoromethyl)phenyl]-2,3,6,9-tetrahydro-3-(hydroxymethyl)-7-methyl-methyl ester 1,1,4,4-tetraoxide.

33. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-[2-fluoro-3-(trifluoromethyl)phenyl]-2,3,6,9-tetrahydro-3-(hydroxymethyl)-7-methyl-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,4,4-tetraoxide.

34. The compound of Claim 1 which is: 5*H*-1,4-Dithiepino[6,5-b]pyridine-8-carboxylic acid, 2,3,6,9-tetrahydro-3-(hydroxymethyl)-7-methyl-9-(3-nitrophenyl)-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,4,4-tetraoxide.

35. The compound of Claim 1 which is: 2*H*,6*H*-1,5-Dithiocino[3,2-*b*]pyridine-9-carboxylic acid, 3,4,7,10-tetrahydro-8-methyl-10-(3-nitrophenyl)-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,5,5-tetraoxide.

36. The compound of Claim 1 which is: 2*H*,6*H*-1,5-Dithiocino[3,2-*b*]pyridine-9-carboxylic acid, 10-[2-fluoro-6-(trifluoromethyl)phenyl]-3,4,7,10-tetrahydro-8-methyl-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,5,5-tetraoxide.

37. The compound of Claim 1 which is: 2*H*,6*H*-1,5-Dithiocino[3,2-*b*]pyridine-9-carboxylic acid, 3,4,7,10-tetrahydro-8-methyl-10-(pentafluorophenyl)-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,5,5-tetraoxide.

38. The compound of Claim 1 which is: 2*H*,6*H*-1,5-Dithiocino[3,2-*b*]pyridine-9-carboxylic acid, 10-[2-fluoro-3-(trifluoromethyl)phenyl]-3,4,7,10-tetrahydro-8-methyl-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,5,5-tetraoxide.

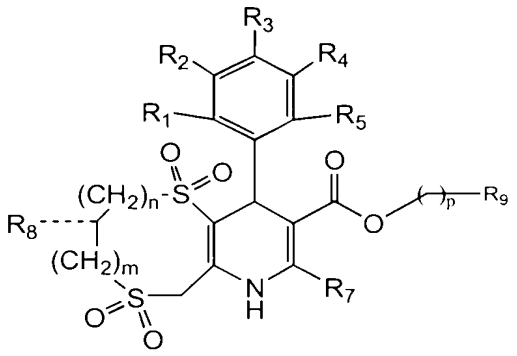
39. The compound of Claim 1 which is: 2*H*,6*H*-1,5-Dithiocino[3,2-*b*]pyridine-9-carboxylic acid, 10-(2-chlorophenyl)-3,4,7,10-tetrahydro-8-methyl-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,5,5-tetraoxide.

40. The compound of Claim 1 which is: 2*H*,6*H*-1,5-Dithiocino[3,2-*b*]pyridine-9-carboxylic acid, 3,4,7,10-tetrahydro-8-methyl-10-(2-nitrophenyl)-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,5,5-tetraoxide.

41. The compound of Claim 1 which is: 4*H*-1,3-Dithiino[5,4-*b*]pyridine-7-carboxylic acid, 8-[2-fluoro-3-(trifluoromethyl)phenyl]-5,8-dihydro-6-methyl-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,3,3-tetraoxide.

42. The compound of Claim 1 which is: 4*H*-1,3-Dithiino[5,4-*b*]pyridine-7-carboxylic acid, 8-(2-chlorophenyl)-5,8-dihydro-6-methyl-2-[methyl(phenylmethyl)amino]ethyl ester 1,1,3,3-tetraoxide.

43. A compound of Formula (II),



II

or a pharmaceutically acceptable salt thereof, wherein

(a) R_1, R_2, R_3, R_4 and R_5 are independently selected from the group consisting of H, OH, halogen, cyano, NO_2, alkyl, C_{1-8} alkoxy, C_{1-8} alkylsulfonyl, C_{1-4} carboalkoxy, C_{1-8} alkylthio, difluoromethoxy, difluoromethylthio, trifluoromethyl, and oxadiazole (formed by R_1 and R_2);

(b) R_7 is selected from the group consisting of H, amino, alkyl, aryl, trifluoromethyl, alkoxymethyl, 2-thieno and 3-thieno;

(c) R_8 is connected to the bis-sulfone ring via a single or double bond, as applicable, and is selected from the group consisting of H, alkylhydroxy, alkenyl, amino, phenyl, benzyl, C_{1-8} straight or branched alkyl, trifluoromethyl, alkoxymethyl, C_{3-7} cycloalkyl, substituted benzyl, formyl, acetyl, t-butyloxy carbonyl, propionyl, substituted alkyl and R'''CH_2C=O, wherein (i) said substituted benzyl is substituted with halogen, trifluoromethyl, C_{1-8} straight and/or branched alkyl or C_{1-8} alkoxy, (ii) said substituted alkyl is substituted with amino, dialkyl amino, C_{1-8} alkoxy, hydroxy and/or halogen, and (iii) R''' is amino, dialkyl amino, C_{1-8} alkoxy, hydroxy or halogen;

(d) R_9 is selected from -alkyl-OH, alkylamine, lactone, cyclic carbonate, alkyl-substituted cyclic carbonate, aryl-substituted cyclic carbonate, –aryl–C(O)OR', –alkyl-aryl–C(O)OR', –alkyl–OC(O)R', –alkyl–C(O)R', –alkyl–C(O)OR', –alkyl–N(R")C(O)R', and –alkyl–N(R")C(O)OR', wherein

R^{I} and R^{II} are independently selected from the group consisting of hydrogen, amino, alkyl, aryl, aryl-fused cycloalkyl, and heterocyclyl, the amino, alkyl, aryl, aryl-fused cycloalkyl, and heterocyclyl being optionally substituted with halogen, cyano, NO_2, lactone, amino, alkylamino, aryl-substituted alkylamino, amide, carbamate, carbamoyl, cyclic carbonate, alkyl, halogen-substituted alkyl, arylalkyl, alkoxy, heterocyclyl and/or aryl (the aryl being optionally substituted with OH, halogen, cyano, NO_2, alkyl, amino, dimethylamino, alkoxy, alkylsulfonyl, C_{1-4} carboalkoxy, alkylthio and/or trifluoromethyl);

(e) m, n, and their sum are each an integer from 0 to 4; and

(f) p is an integer from 0 to 4.

44. The compound of Claim 43, wherein R_9 is –aryl-alkyl–OC(O)R'.

45. The compound of Claim 43, wherein R_9 is –alkyl–N(R")C(O)R'.

46. The compound of Claim 45 which is: 5*H*-[1,4]dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2-chloro-6-fluorophenyl)-2,3,6,9-tetrahydro-7-methyl-, 2-[[(1,1-dimethylethoxy)carbonyl]amino]ethyl ester, 1,1,4,4-tetraoxide.

47. The compound of Claim 43, wherein R_9 is –alkyl–OC(O)R'.

48. The compound of Claim 47 which is: 5*H*-[1,4]dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2-chloro-6-fluorophenyl)-2,3,6,9-tetrahydro-7-methyl-, 2-[[(1,2,3,4-tetrahydro-2-naphthalenyl)carbonyl]oxy]ethyl ester, 1,1,4,4-tetraoxide.

49. The compound of Claim 47 which is: 5*H*-[1,4]dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2-chloro-6-fluorophenyl)-2,3,6,9-tetrahydro-7-methyl-, 2-[(cycloheptylcarbonyl)oxy]ethyl ester, 1,1,4,4-tetraoxide.

50. The compound of Claim 47 which is: 5*H*-[1,4]dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2-chloro-6-fluorophenyl)-2,3,6,9-tetrahydro-7-methyl-, 2-[[4-(1-methylethoxy)benzoyl]oxy]ethyl ester, 1,1,4,4-tetraoxide.

51. The compound of Claim 47 which is: 5*H*-[1,4]dithiepino[6,5-*b*]pyridine-8-carboxylic acid, 9-(2,3-dichlorophenyl)-2,3,6,9-tetrahydro-7-methyl-, 2-(2-methyl-1-oxopropoxy)ethyl ester, 1,1,4,4-tetraoxide.

52. The compound of Claim 47 which is: 2*H*,6*H*-[1,5]dithiocino[3,2-*b*]pyridine-9-carboxylic acid, 10-(2-chloro-6-fluorophenyl)-3,4,7,10-tetrahydro-8-methyl-, 2-[[4-(1-methylethoxy)benzoyl]oxy]ethyl ester, 1,1,5,5-tetraoxide.

53. A pharmaceutical composition comprising the compound of Claim 1 or 43 and a pharmaceutically acceptable carrier.

55. A method of inhibiting in a subject the onset of a disorder whose alleviation is mediated by the reduction of calcium ion influx into cells whose actions contribute to the disorder, which method comprises administering to the subject a prophylactically effective dose of the pharmaceutical composition of Claim 53.

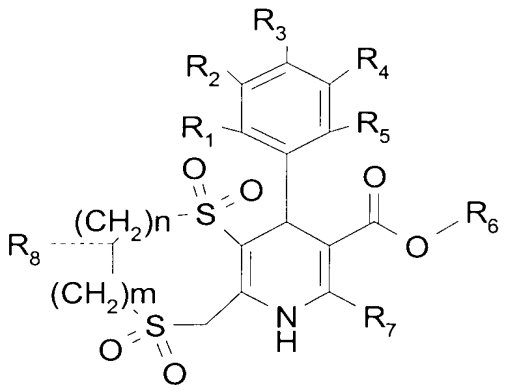
56. The method of Claim 54 or 55, wherein the disorder is selected from the group consisting of hypersensitivity, allergy, asthma, bronchospasm, dysmenorrhea, esophageal spasm, glaucoma, premature labor, a urinary tract disorder, a gastrointestinal motility disorder and a cardiovascular disorder.

58. The method of Claim 56, wherein the cardiovascular disorder is selected from the group consisting of hypertension, ischemia, angina, congestive heart failure, myocardial infarction and stroke.

59. An apparatus for administering to a subject the pharmaceutical composition of Claim 53, comprising a container and the pharmaceutical composition therein, whereby the

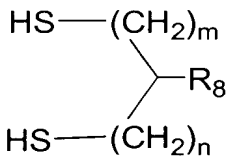
container has a means for delivering to the subject a therapeutic and/or prophylactic dose of the pharmaceutical composition.

60. A process for preparing the compound of Claim 1

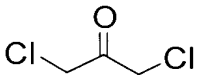


wherein m, n, and their sum are each an integer from 1 to 4, which process comprises the steps of

(a) reacting the compound of Formula 1a with the compound of Formula 1b

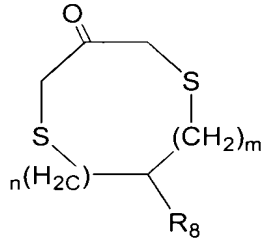


1a



1b

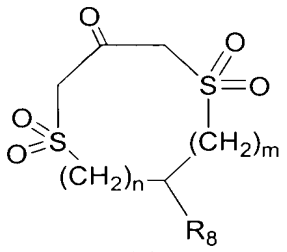
to form the compound of Formula 1c;



1c

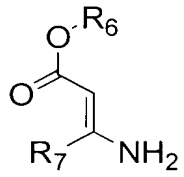
(b) reacting the compound of Formula 1c with m-chloroperoxybenzoic acid to form the compound of Formula 1d;

and

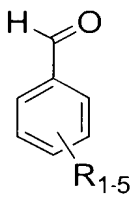


1d

(c) reacting the compound of Formula 1d with the compounds of Formulae 1e and 1f



1e

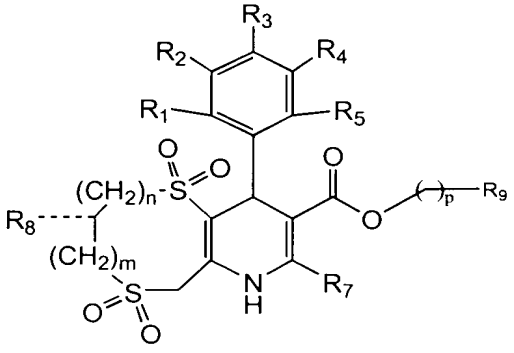


1f

to form the compound of Claim 1.

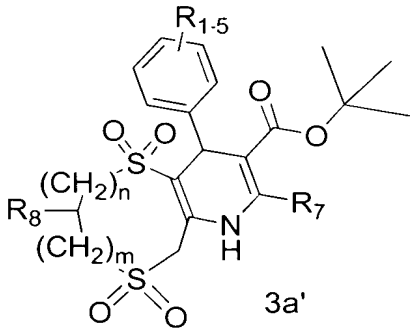
61. The process of Claim 60, wherein R_8 of the compound of Formula I is a methylene group formed from a methylol group using a dehydrating agent.

62. A process of preparing the compound of Claim 43,

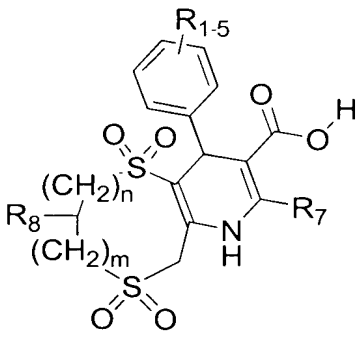


which process comprises the steps of

(a) reacting the compound of Formula 3a' with formic acid to form the compound of Formula 3b'; and



3a'



3b'

(b) reacting the compound of Formula 3b with R_9Br or R_9Cl to form the compound of Claim 43.

63. The process of Claim 62, wherein R_7 is methyl.